ON THE ABSORPTION OF FLUIDS FROM THE CONNECTIVE TISSUE SPACES. By ERNEST H. STARLING. (Two Figures in Text.)

(From the Physiological Laboratory, Guy's Hospital.)

UNTIL within the last few years, all workers, who investigated the question of absorption by the blood vessels, confined their experiments to cases in which some substance, not occurring normally in the blood, was introduced into some connective tissue space. That, under these conditions, absorption by the blood vessels does take place, was shown by Majendie, and confirmed in recent years by Ascher[1] as well as by Tubby and myself[2]. Although the ease, with which this interchange by a process of diffusion between blood and extravascular fluids takes place, must be of great importance for the normal metabolism of the tissues (as, *e.g.* the much discussed supply of CaO to the mammary gland-cells), yet such processes will not serve to explain the absorption by the blood vessels of fluids having the same tonicity and the same approximate constitution as the circulating plasma. The fluids contained in the tissue-spaces have the same tonicity and the same composition in salts as blood-plasma. We have to inquire first whether the blood vessels do absorb such isotonic fluids, and secondly the manner in which this absorption takes place.

EVIDENCE AS TO ABSORPTION BY BLOOD VESSELS.

1. *Absorption from the serous cavities.*

A number of experiments have been made recently on the subject of the absorption of isotonic fluids (*e.g.* 1 % salt solution or serum) from the serous cavities. Orlow[3] showed that isotonic fluids were absorbed from the peritoneal cavity with considerable rapidity without producing any corresponding lymph-flow from the thoracic duct, and concluded

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[1] *Zeitschrift f. Biologie,* 1893. 247.   [2] This *Journal,* XVI. 140. 1894.
[3] *Pflüger's Archiv,* LIX. 170. 1894.

that the fluid was absorbed by means of the blood vessels and that the cells lining the cavity took an active part in the process. His experiments were repeated on the pleura and the peritoneum by Leathes[1] and myself and by Hamburger[2]. We found that 1 % salt solution was taken up fairly rapidly (5 to 10 c.c. an hour) from the pleura. We were unable to decide as to the channels of this absorption; but, from the fact that it went on as usual when a poisonous isotonic solution of sodium fluoride was used, concluded that the absorption must be due to some mechanical or physical condition. Hamburger showed that fluids might be taken up even from the peritoneum of a dead animal. In a recent paper Cohnstein[3], drawing attention to the fact that, after injection of fluid into the peritoneum, we may get a slow slight increase in the lymph-flow from the thoracic duct, concludes that the lymphatics are the sole channels of absorption. I have attempted to decide the question as to the channels of absorption by observing the fate of injected fluids after ligature of the thoracic duct on both sides, combined, in some instances, with ligature of the right innominate vein. Although I have made a number of such experiments in which the fluids were absorbed from the serous cavities, I could never be certain that the pathway by the lymphatics had been blocked by my ligatures. In all cases, carmine which had been injected into the peritoneal cavity some time after the ligature of the ducts, was found in the anterior mediastinal glands, as well as in a gland near the root of the right side of the neck, pointing to the existence of a current of lymph upwards through these glands. I may quote here one of these experiments as an example of the series.

Oct. 11th, 1895. Dog about 10 kilos. Left thoracic duct and right-lymphatic duct ligatured. Right innominate vein ligatured. Then injected 500 c.c. 1 % NaCl solution into peritoneal cavity.

Oct. 12th. Injected 300 c.c. of suspension of carmine in 1 % NaCl solution into peritoneal cavity.

Oct. 14th. Dog killed. All fluid absorbed. No carmine in the distended thoracic duct or in retroperitoneal glands. Carmine present in anterior mediastinal glands and in a gland in neighbourhood of right lymphatic duct.

We must conclude therefore that it is impossible by this method to obtain a definite answer to the question whether blood vessels can absorb isotonic fluids.

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[1] This *Journal*, xviii. 106. 1895.   [2] *Du Bois' Archiv*, 1895. 281.
[3] *Centralblatt f. Physiol.* Sept. 21, 1895.

2. *Effects of artificial anæmia.*

There are however certain facts which have been known to physiologists for the last fifty years and which, to my mind, prove conclusively the absorption by the blood vessels of the fluids in the connective tissue spaces.   If an animal be bled to a certain amount, the remaining blood very shortly afterwards is found to be more dilute than before.   It contains less hæmoglobin and blood corpuscles and relatively more plasma.   The plasma is also more dilute than before, showing that the increase in volume of blood chiefly consists of added water and salts, or at any rate, a fluid which contains less proteid than the plasma.   In older works on physiology, we find this dilution of the blood ascribed to an increased flow of lymph from the thoracic duct into the blood.   The result of bleeding, however, is to diminish the flow of lymph from the thoracic duct, and the dilution of the blood takes place just as well when the lymph is being led away by a cannula inserted in the duct. As an example of this change I may quote the following figures given by Tscherewkow[1].

(1) Dog 11·4 kilos.   Withdrawal of 220 c.c. blood reduced solids of serum from 7·72 % to 7·14 %.

(2) Dog 6·5 kilos.   Withdrawal of 150 c.c. blood reduced solids of serum from 7·77 % to 6·47 %.

I have made some experiments to ascertain whether this absorption of fluid is effected only in the abdominal viscera, or whether it may take place in the connective tissues of the peripheral parts of the body.

I find that after *total extirpation* of the abdominal viscera, the organism reacts in the same way as in a normal animal to a considerable bleeding.   We may conclude therefore that this absorption of fluid by the blood vessels, after bleeding, takes place throughout the body.   This conclusion is also borne out by the experiments of Dr Lazarus Barlow[2] on the specific gravity of the tissues.

3. *Absorption of an artificial œdema.*

In order to put the fact of absorption of isotonic fluids by the blood vessels beyond all doubt, and to exclude all possibility of the concurrence of lymphatics in this process, I have carried out the following experiment.

[1] *Pflüger's Archiv*, LXII. 304. 1895.
[2] *Proc. Physiol. Soc.* 1894. (This *Journal*, XVI. p. xiii.)

The blood of a dog was defibrinated inter vitam, by bleeding, whipping and reinjecting the blood five or six times. [This was to avoid the danger of capillary clots during the subsequent experiment.] The dog was then bled to death, and cannulæ inserted in the femoral arteries and veins on both sides. The right leg was then made œdematous by the injection of 1 % or 1·05 % NaCl solution into the connective tissues by means of a needle. Part of the blood which had been obtained having been set aside for subsequent analysis, the rest was divided into two equal parts. One-half was then led through each limb at a pressure varying between 65 and 85 mm. Hg. By means of an arrangement of tubes and clamps, somewhat similar to that of Ludwig's 'Stromaiche,' it was possible, as soon as all the blood had been led through, to start the circulation afresh from the bottle which had been previously connected with the vein. I was thus carrying on two experiments (one of them being a control) at the same time. Each half of the blood was led through one leg from 12 to 25 times. At the end of this time, the experiment was stopped, and the solids in the whole blood and serum of the three samples of blood estimated, as well as the relative amounts of hæmoglobin in each. It will be seen that the blood, which had been led through the normal leg from 12 to 25 times, was either unaltered, or, as in most cases, underwent slight concentration. The blood which had been led the same number of times through the œdematous leg had in all cases absorbed fluid: both the whole blood and the serum were more dilute and the hæmoglobin percentage was diminished. In these experiments the freezing points of the blood-serum and of the fluid injected to form the œdema, were estimated and care was taken to ensure that the osmotic pressure of the injected fluid was not below that of the blood-serum, so that the absorption of the fluid could not be explained by ordinary osmotic processes. I give here a table showing the results of these experiments.

As the result of these experiments, we may affirm with certainty that isotonic salt solutions can be taken up directly by the blood circulating in the blood vessels.

No. of Exp.	Solids of Blood per cent.			Haemoglobin (standard = 100)		Solids of serum and freezing points			Composition of oedema fluid and freezing point	No. of times blood transfused through legs
	Standard	From normal leg	From oedematous leg	Blood from normal leg	Blood from oedematous leg	Standard	Normal leg	Oedematous leg		
I	21·00	21·08	19·98	—	—	—	6·6 % $\Delta = -\cdot635$	6·1 % $\Delta = -\cdot635$	1 % NaCl $\Delta = -\cdot610°$ C.	12 times
II	18·9	19·2	18·5	—	—	—	—	—	1 % NaCl	16 ,,
III	22·2	22·2	21·4	—	—	—	7·2 % $\Delta = -\cdot640$	6·7 %	1 % NaCl $\Delta = -\cdot610°$ C.	12 ,,
IV	lost	20·1	19·4	—	—	—	—	—	1·05 % NaCl	12 ,,
V	20·6	(no control)	20·00	—	—	—	—	—	1·05 % NaCl	12 ,,
VI	21·26	21·42	20·56	100	97	—	—	—	1·1 % NaCl	20 ,,
VII	19·97	20·66	19·75	104	96	—	8·28 % $\Delta = -\cdot64$	7·71 % $\Delta = -\cdot64$	1·1 % NaCl $\Delta = -\cdot660°$ C.	24 ,,
VIII	20·7	21·2	20·00	103	95	$\Delta = -\cdot600$	$\Delta = -\cdot615$	$\Delta = -\cdot63$	1·03 % NaCl $\Delta = -\cdot640°$ C.	20 ,,

Two Experiments with Serum

No. of Exp.	Standard	From normal leg	From oedematous leg	Blood from normal leg	Blood from oedematous leg	Standard	Normal leg	Oedematous leg	Composition	No. of times
IX	21·12	21·08	21·09	—	102	—	$\Delta = -\cdot605$	$\Delta = -\cdot605$	Ox serum $\Delta = -\cdot580°$ C.	15 times
X	19·5	19·9	19·7	102	102	—	$\Delta = -\cdot645$	$\Delta = -\cdot635$	Ox serum $\Delta = -\cdot585°$ C.	15 ,,

MECHANISM OF ABSORPTION BY THE BLOOD VESSELS.

We have now to consider how this absorption is effected. Are the capillary walls so constituted as to react to a lowering of the capillary pressure with an active absorption of extravascular fluid, *i.e.* is the absorption due to vital activity of the cells? or can we find mechanical conditions that will account for this absorption?

The first possibility that will strike anyone working at the subject is that the absorption, like the transudation, of fluid, may be effected by a process analogous to filtration. Landerer[1] estimated the tissue tension at half to three-quarters of that existing in the capillaries. It is evident that, if such were the case, any considerable fall of intra-capillary pressure would bring it below the tissue-pressure, and a back-filtration into the vessels might occur. Some experiments of Klemensiewicz[2] with regard to the mechanical effects of œdema on the circulation might be quoted against this hypothesis. This latter observer led fluid through a piece of intestine enclosed in an outer tube of glass. He found that at first there was transudation outwards through the intestinal wall and a rise of pressure in the glass tube. As soon however as the pressure in the outer tube reached that obtaining at the venous end of the model capillary, this latter collapsed. Exudation continued however to go on from the arterial end of the capillary. The pressure therefore rose higher and higher in the outer tube until the exuded fluid had caused collapse of the greater part of the intestinal tube. He concluded that a similar sequence of events would take place in œdema and that the exuded fluid would tend to compress the veins, thus raising the pressure in the capillaries still higher and increasing the exudation. A vicious circle was thus established, which only ended with the complete arrest of the circulation through the part affected.

This objection of Klemensiewicz to the possibility of filtration backwards only holds good if the structural relations in the connective tissues are similar to the arrangement of his mechanical model. If however the capillaries, instead of running freely through the connective tissue spaces, are bound to the walls of these spaces by an adventitia of radiating fibres, a rise of pressure in the spaces above that obtaining in

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[1] *Die Gewebsspannung in ihrem Einfluss auf die örtliche Blut- und Lymphbewegung.* Leipzig, 1884.

[2] *Sitzb. der k. Akad. der Wissensch.* LXXXIV. 1881 and XCIV. 1886.

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the capillaries will not collapse these latter, but will rather tend to dilate them; and filtration back into the capillary would be structurally possible. If sections be cut of injected œdematous connective tissues, it will be seen that the capillaries are surrounded and supported by such an adventitia of radiating fibres, and have in fact a structure very similar to that figured by Ranvier[1] in the lymphatic gland and by Heidenhain[2] in the section through a villus. In the veins however no such arrangement can be seen, all the fibres surrounding these tubes being apparently disposed concentrically. From a purely anatomical study, it would seem therefore that a filtration back into the capillaries is possible, provided that the rise of pressure in the tissue spaces does not extend to the tissues surrounding the larger veins. It is evident however that the question whether filtration back into the vessels is or is not possible from the connective tissues in most parts of the body, can be only definitely solved by physiological experiment.

I attempted at first to decide this question by observing the capillary circulation in the tongue and web of the frog, while I injected fluid into these parts at a pressure equal to the aortic pressure, which was measured at the same time. In both these localities the production of œdema in this way seemed to leave the capillary circulation unaffected or even to cause a certain quickening. The experiments however were not satisfactory, since it was impossible to ascertain what relation the pressure in the connective tissue spaces bore to the pressure used in injecting the fluid through a fine needle. I therefore devised the following experiment. In a medium-sized dog the blood was first defibrinated intra vitam. A T cannula was then inserted into one of the veins on the dorsum of the foot and connected with a manometer containing normal saline. A cannula was inserted in the internal saphenous vein in the upper part of the thigh and blood allowed to flow away through this; the outflow of blood being measured in graduated cylinders. A needle, connected with a pressure bottle containing warm normal saline, was run into the connective tissue of the leg about one inch in front of the situation of the internal saphenous vein. Two Southey's tubes were also inserted in the connective tissue, one tube (*C*) about 1½ inches from the point of the injecting needle on the other side of the vein, and the other tube (*D*) on the same side of the vein as the injecting needle, but 2 inches nearer the knee. Both these tubes were connected with water manometers. At the same time

[1] *Technisches Lehrbuch der Histologie* (Nicati und Wyss), Fig. 208. 1877.
[2] Cp. *Quain's Anatomy*, 10th Ed. III. Pt. 4. Fig. 110.

the arterial pressure was taken by means of a mercurial manometer connected with the femoral artery of the other leg. The arrangement of the needles and cannulæ is indicated in the accompanying diagram.
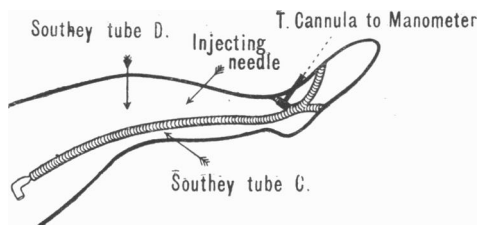
I give here the results of one such experiment.

May 1, 1895. Dog about 7 kilos. Cannulæ arranged as in Diagram.

Pressures (mm. water).

Time	Vein of foot	Injecting needle	Southey tube C	Southey tube D	Flow in previous 10 mins.
2.25	—	—	—	—	4·2 c.c.
2.35	122	—	—	—	2·8 „
2.50	118	—	—	—	2·8 (15 mins.)
3.0	108	—	—	—	1·8 c.c.
3.10	103	—	—	—	1·5 „
3.10	Injection of 1 % NaCl into connective tissue begun				
3.20	105	315	—	—	1·3 c.c
3.30	?	315	—	155	0·8 „
3.40	133	355	145	155	0·4 „
3.50	170	265	157	165	0·4 „
3.50	Injection stopped				
4.0	120	107	103	97	0·5 „
4.15	110	80	80	70	1·8 (15 mins.)
4.15	Injection recommenced				
4.25	183	235	130	155	1·3 c.c.
4.40	220	245	160	180	1·8 (15 mins.)
4.40	Injection stopped				
4.50	160	110	110	102	1·3 c.c.
5.0	145	93	97	88	1·6 „
5.10	137	80	95	75	1·8 „
5.20	132	76	87	68	2 „
5.30	127	70	85	67	2·4 „

It will be seen that, with the rise of pressure in the connective tissues, the pressure in the veins of the foot rose, while the outflow from the cannula in the saphenous vein fell, showing conclusively that the effect of a rise of pressure in the connective tissue spaces of the leg is to cause collapse of the big veins and therefore increased pressure in the peripheral veins and capillaries. It is evident therefore that, in the leg, the conditions are analogous to those in Klemensiewicz' experiment.

It seemed possible however that filtration might still occur in other tissues of the body, such as muscular or glandular structures. I carried out therefore similar experiments to those described on the leg, on the submaxillary gland as a type of glandular, and on the tongue as a type of muscular structure. Although these experiments are not so complete as those on the leg, owing to the impossibility of measuring the pressure in the veins peripheral to the œdema, I found that the invariable result of the production of an œdema in these parts was to diminish the outflow of blood. In order to be certain in the case of the tongue that the arterial pressure should be constant throughout, I defibrinated the animal, killed it by bleeding, and then led defibrinated blood at a known pressure through the vessels of the tongue. I had previously divided all the nerves going to the tongue in order, as far as possible, to obviate any changes occurring in the calibre of the arteries.

From these experiments we may conclude that an absorption of fluid by the blood vessels by a process of backward filtration is impossible in the connective tissues of the limbs, in muscles, and in all glandular structures which have an analogous build to the sub-maxillary gland. Theoretically we may say that absorption by filtration is only possible in those regions of the body where a sudden rise in tissue-pressure will not be propagated to the neighbourhood of the larger veins[1]. Of the existence of such regions however we have no experimental evidence[2].

Hamburger has sought to explain absorption of isotonic fluids from the serous cavities by ascribing it to capillary and molecular 'imbibition.' The difficulty in this explanation is the significance which is to be bestowed on the word imbibition. This term for instance is applied to

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[1] This argument does not of course apply to the cranium, where the veins are always patent and where, as Hill has shown, filtration of cerebro-spinal fluid into the veins may take place.

[2] The intestinal villus might possibly afford an example of such a structure.

the absorption of fluids by porous bodies, such as animal charcoal. Now such a process may be concerned in the dispersal of the fluid through the interstices of the tissues surrounding the serous cavities, but it is difficult to see how it would lead to the taking up of the fluid by the circulating blood, nor would it explain the delicate balance which has been shown to exist between the volume of circulating blood and intra-capillary pressure, and the absorption from or transudation into the con-nective tissue-spaces. On the other hand, molecular imbibition, *e.g.* the process by which gelatin will take up water and salts from proteid solutions, may possibly be of the same nature as the process which I am about to describe and which I think is the predominant factor in the absorption of isotonic fluids by the blood vessels.

I believe the explanation is to be found in a property on which much stress was laid by the older physiologists, and which they termed the high endosmotic equivalent of albumen. It must be remembered that the earlier workers used animal membranes in their experiments on osmotic interchanges. These membranes permit the passage of water and salts, but hinder the passage of coagulable proteid. The application of semi-permeable membranes by Pfeffer to the measure-ment of osmotic pressures, showed that the osmotic pressures of salts and other crystalloids are enormously higher than those of such substances as albumen, and it has therefore been supposed that the osmotic pressure of the proteids in serum being so insignificant must be of no account in physiological processes. The reverse is however the case. Whereas the enormous pressures of the salts and crystalloids in the various fluids of the body are of very little importance for the function of absorption by the blood vessels, the comparatively insignifi-cant osmotic pressure of the albumens is I believe of great importance, and for this reason.
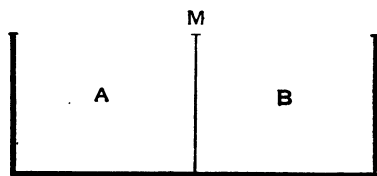
Supposing we have two vessels *A* and *B*, containing salt solutions of different strength, separated by a membrane *M*, which is easily perme-able to water and salts. If we imagine that *A* is the more concentrated, there will be a passage of water from *B* to *A*, and the force with which

this attraction of water is effected will be equal to the difference between the osmotic pressures on both sides of the membrane. Now since the membrane is freely permeable to salt, there will also be a passage of salt from *A* to *B*. The layer of fluid in immediate contact with the *A* side of *M* will be therefore less concentrated than *A*, while that in immediate contact with the *B* side of *M* will be more concentrated than *B*; that is to say, the fact that diffusion can take place readily through the membrane minimises the effect of the original difference of osmotic pressures on the transference of fluid. The fluids on the two sides will in time attain equal concentrations; the amount of fluid, *i.e.* water, transferred in the process, diminishing as the diffusibility of the salt increases. Supposing now we add to *A* some substance to which the membrane is impermeable, which we may denote *X*. Since this cannot pass through the membrane, it will exert an osmotic attraction on the water in *B*. Water will flow from *B* to *A* and *B* will become slightly more concentrated. We have now two opposing osmotic forces: the osmotic pressure of *X* in *A* and the osmotic pressure of the excess of salt in *B*. This would tend to produce a position of equilibrium were it not that the condition of excess of salt on one side of a membrane which is permeable to it is an unstable one. The excess of salt must diffuse into *A* and we get a re-establishment of the osmotic difference determined by the presence of *X* in *A*. The final result therefore must be that *A* absorbs the whole of *B*.

Now this illustration represents to some extent conditions existing in the living body. In the limbs and connective tissues generally of the peripheral parts of the body, we have capillaries which are more or less impervious to proteids. As the blood passes under pressure through these capillaries, a certain amount of lymph is filtered through their walls, but in the process it loses the greater part of its proteids. We have therefore on one side of the capillary wall blood-plasma with 8 % proteids, on the other side lymph containing 2 to 3 % proteids. In this separation of proteid a certain amount of work must have been done, and if the proteids of serum are really analogous to the substance *X* of my illustration and possess an osmotic pressure, there must be a difference of osmotic pressure between intra- and extravascular fluids tending to a reabsorption of the latter. It becomes desirable to inquire whether the proteids of serum have any osmotic pressure and if so, what is the extent of this pressure.

To decide these points I have attempted to measure the osmotic pressure of the proteids in the serum directly. The osmometer consists

of a small glass bell provided near the top with two vertical tubulures. Over the mouth of the bell is tied a peritoneal membrane similar to that used by Dr Lazarus Barlow. This was however rendered absolutely watertight by soaking it for some minutes, after it had been tied on, in a 10 % solution of gelatin. The membrane is prevented from bulging by fixing over it a perforated silver or copper plate. The wider of the two tubulures is used for filling the bell with serum. The other one is connected either with a long narrow tube, or with a small mercurial manometer. Three or four of these osmometers are fixed in a wooden disc and arranged to revolve in alternating directions by means of a kitchen jack with their lower ends immersed in salt solution. The salt solution was in most cases 1·03 % NaCl and was therefore slightly hypertonic to the serum.

In all my experiments the fluid in the osmometer began to rise in the tube within two or three hours after the commencement of the experiment, and rose steadily for 3 or 4 days, the final height varying from 30 to 41 mm. Hg. I give here details of two of these experiments.

I.   Jan. 27, 1896.   Started an osmosis experiment; two osmometers (C and D) containing serum, while B contained a mixture of about $\frac{2}{3}$ serum and $\frac{1}{3}$ outer fluid.   Outer fluid = 1 % NaCl.   Fluid forced up in the osmometers to heights varying from 3 to 6 inches.   A few hours later the fluid in all osmometers had sunk about $\frac{1}{4}$ inch.

Jan. 29.   Height of fluid in C and D = 13 inches = 32·5 cm.

Height of fluid in B = 9 inches = 22·5 cm.

Δ of outside fluid at beginning of exp.   = − ·605° C.

,,   ,,   at end   ,,   = − ·615 ,,

Δ of serum in C and D at beginning   = − ·605 ,,

,,   ,,   ,,   at end   = − ·615 ,,

(The outer fluid, being exposed to the air, concentrated by evaporation during the course of the experiment.)

II.   Feb. 4, 1896.   Three osmometers filled with serum.

A.   Pressure raised to 60 cm. serum.   This fell to 53 cm. in 30 mins. and to 50 cm. after 2 hrs.

B.   Connected with Hg. manometer.   Pressure started at 56 min.

C.   Left open.

Feb. 5.   (24 hrs later.)   At 11 a.m.

Height of A = 53 cm. (serum).

Height of B = 40 mm. Hg.

C had overflowed.

Feb. 5.   At 4 p.m.
    Height of A = 53 cm. serum.
    Height of B = 40 mm. Hg.
    Height of C = 15 cm. serum.   Experiment stopped.
At beginning of experiment Δ of serum   = $-$ ·600° C.
      ,,   ,, Δ of outer fluid (1·03 % NaCl) = $-$ ·630° C.
At end of experiment Δ of serum   = $-$ ·635° C.
     ,,   ,, Δ of outer fluid = $-$ ·635° C.
The serum contained 7·56 % proteids.

The importance of these measurements lies in the fact that, although the osmotic pressure of the proteids of the plasma is so insignificant, it is of an order of magnitude comparable to that of the capillary pressures; and whereas capillary pressure determines transudation, the osmotic pressure of the proteids of the serum determines absorption. Moreover, if we leave the frictional resistance of the capillary wall to the passage of fluid through it out of account, the osmotic attraction of the serum for the extravascular fluid will be proportional to the force expended in the production of this latter, so that, at any given time, there must be a balance between the hydrostatic pressure of the blood in the capillaries and the osmotic attraction of the blood for the surrounding fluids. With increased capillary pressure there must be increased transudation, until equilibrium is established at a somewhat higher point, when there is a more dilute fluid in the tissue-spaces and therefore a higher absorbing force to balance the increased capillary pressure. With diminished capillary pressure there will be an osmotic absorption of salt solution from the extravascular fluid, until this becomes richer in proteids; and the difference between its (proteid) osmotic pressure and that of the intravascular plasma is equal to the diminished capillary pressure.

Here then we have the balance of forces necessary to explain the accurate and speedy regulation of the quantity of circulating fluid. It is evident however that we cannot explain in this way the absorption of serum or other fluids rich in proteids from the serous cavities and connective tissues. I would point out however that we have as yet no sufficient evidence that such fluids are absorbed by the blood vessels. If we inject serum into the pleural cavity we find that it is absorbed very much more slowly than is a similar amount of salt solution. The absorption is indeed so slow that it is impossible to exclude the possibility that the whole of it has taken place through the lymphatics.

In two experiments in which I made the limb œdematous with serum instead of salt solution, I could obtain no evidence of absorption of the œdema fluid by the blood vessels. Details of these experiments are given at the end of the table on page 316. The extreme slowness with which inflammatory exudations, *i.e.* fluids rich in proteids, are absorbed in man, also tells against the absorption of these fluids being effected directly by the blood vessels. It is evident however that, if serum be diffused through the meshes of a tissue, the cells of the tissue will feed on the proteids of the serum. As the serum becomes in this way more dilute, its water and diffusible constituents may be taken up by the blood vessels. So far as I know there is no physical process other than filtration by which the absorption of proteids by the blood vessels could be effected. Filtration is excluded by my experiments in the case of the connective tissues of the limbs and peripheral parts of the body, so that a proof that proteids are absorbed in these situations would point to an active intervention of the endothelial cells in the process. All the physiological facts however which are so far definitely ascertained can be explained by the physical processes mentioned in this paper.

Conclusions.

1. Salt solutions, isotonic with the blood-plasma, can be and are absorbed directly by the blood vessels. This statement probably holds good for dropsical fluids containing small percentages of proteids.

2. A backward filtration into the vessels is mechanically impossible in the connective tissues of the limbs, of the muscles and of the glands similar in structure to the submaxillary.

3. The proteids of serum have an osmotic pressure of about 30 mm. to 40 mm. Hg. Absorption of isotonic salt solutions by the blood vessels is determined by this osmotic pressure of the serum proteids. The same factor is probably responsible for the absorption from the tissues which ensues on any general lowering of capillary pressures, *e.g.* artificial anæmia.

4. The proteids of the tissue fluids, when not used up in the tissues themselves, are probably absorbed mainly, if not exclusively, by the lymphatic system.

Note. It is evident that if we translate the term "molecular imbibition" of Hamburger by osmotic pressure of the proteids of the tissues and blood, the explanation of absorption given in the above paper is practically identical with that proposed by this observer.

I must regret the more therefore that in Hamburger's latest contribution to the subject[1], the question is obscured by a mechanical illustration which can have little or no significance for the process of absorption by the blood vessels. In this experiment he has two concentric tubes, the outer one of glass, the inner one of gelatin in the meshes of a nickel gauze cylinder. On filling the outer tube with serum and leading serum through the inner tube, he notices that the outer fluid becomes more concentrated, and that fluid is taken up by the serum passing along the inner tube. Now, on referring to the conditions necessary for the success of the experiment, one sees at once that the pressure in the inner tube must be lower than that in the outer tube, so that Hamburger is really in this experiment imitating transudation rather than absorption. As I have shown above, an absorption, which depends on the extravascular pressure being higher than the intravascular pressure, is mechanically impossible in the case of most of the connective tissues of the body.

[1] *Du Bois' Archiv*, 1896. 36.